REMARKS/ARGUMENTS

Claims 1-28 were pending in the subject application. Claims 2 and 4-28 have been canceled herein. Claims 29 and 30 have been added. Accordingly, claims 1, 3, 29 and 30 are presented for examination on the merits.

Claim 1 was amended to incorporate certain limitations from canceled original claims. New claims 29 and 30 are based on the composition claims originally filed with the application. As such, the claims are fully supported and add no new matter.

Applicants thank the Examiner for deleting the duplicated cited reference from the IDS filed on December 28, 2006.

I. Double Patenting Rejection

Claims 1-28 are rejected on the ground of non-statutory obviousness-type double patenting over claims 1-57 of U.S. 7,091,030 and/or U.S. 6,020,172. Applicants do not agree with the Examiner's assertion, but in the spirit of furthering prosecution of the application have amended the claims. It is respectfully submitted that the amendments to the claims and the unexpected results discussed below render this ground of rejection moot.

Accordingly, it is respectfully requested that this ground of rejection be withdrawn.

II. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

Claims 1-28 are rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not provide an enabling disclosure of the claimed invention. In particular, the examiner cites to an alleged problem in the art with targeting tissue in regards to gene therapy treatments. The Examiner asserts that the specification does not provide guidance which would allow the practitioner to use the claimed composition and method for any form of administration other than direct administration into the target tumor.

Applicants disagree with the Examiner's conclusion.

The present invention provides both a composition and a method for treating solid tumors. The Examiner has based the rejection on an alleged absence of evidence that the **method** is operable when the composition is delivered by any means other than direct injection into the tumor, but has not provided an explanation as to how the composition claims are not enabled. The composition claims do not include a method of delivery and therefore, were improperly rejected.

Further, the Examiner asserts that the claimed method will not work over the scope of claimed method, but has not taken into account the fact that the composition used in the claimed method comprises lipids, which have been shown to enhance the uptake by a range of cells. Moreover, methods are known in the art for targeting tumor cells, such as that taught in the specification at page 10, lines 21-24. The skilled practitioner would recognize that tumor specificity can be obtained by including tumor specific antibodies with the cationic lipids. Others have obtained uptake of anti-tumor agents by delivery of the agent into the airway passages, *e.g.* , delivery to lung tumors or tumors in the nasal passages. Thus, the Examiner's assertions that the only method known to work is direct injection into a tumor is inaccurate.

It is respectfully submitted that the rejection of claims 1-28 under 35 U.S.C. § 112, first paragraph is respectfully traversed.

III. Rejections of Claims Under 35 U.S.C. § 103(a)

A. Claims 1-4, 9, 10, 12-14, 16, 17, 22, 23 and 25-27 are rejected under 35 U.S.C. § 103(a) as being obvious over a combination of eighteen cited prior art references. The Examiner relies on each of the cited references as teaching the availability and use of adenovirus vectors or specifically, atadenovirus vectors, the inclusion of a promoter operatively linked to a suicide

gene, the use of such vectors in general to treat prostate cancer, or the use of cationic lipids, such as CSO 87. the Examiner concludes, therefore, that the skilled practitioner would have found it obvious to combine all of the elements taught in these prior art references to develop the claimed composition and methods of its use.

Applicant respectfully disagrees.

As a first matter, it is respectfully pointed out that the rejection specifically does not include claims 6 and 19 (which is directed to use of the probasin promoter); 7 and 20 (directed to use of a transcriptional enhancer element); 8 and 18 (directed to use of a prostate specific membrane antigen gene); or 11 (directed to use of 6-methyl-purine-2 deoxyribose or fludarabine. Since the limitations of each of these non-rejected claims have been added to the amended claims, it is respectfully submitted that the rejection has been traversed.

Furthermore, even if the skilled practitioner were motivated to combine the cited references in the manner suggested by the Examiner, there would have been no expectation that the resulting composition and method provide the enhanced, gene-directed enzyme pro-drug therapeutic effect observed with the claimed invention. The results obtained with the claimed composition and method could not have been predicted on the basis of the cited art. In this regard, Applicant has enclosed herewith four journal articles, three of which were published after the priority date of the subject invention, which demonstrate the unexpected, enhanced activity obtained with the claimed composition and method:

1. Wang et al. (copy enclosed) describes intratunor administration of OAdV623 and the consequent reduction in tumor growth;

2. Martiniello-Wilkes et al (copy enclosed) demonstrate the efficacy of the gene construct (PNP-GDEPT) delivered *via* atadenovirus vector against both local and pseudo metastatic prostate cancer growth in the RMI model;

3. Mariniello-Wilkes (copy enclosed) demonstrate that a single course of OadV-delivered PNP and fluarabine results in suppression of prostate cancer growth in immune-competent TRAMP mice; AND

4. Fasbender et al. (copy enclosed) demonstrate complexes of adenoviruses and cationic lipids increase the efficacy of gene transfer.

Accordingly, in view of the amendments to the claims, as well as the unexpected results obtained with the claimed composition and method, the rejection of claims 1-4, 79, 10, 12-14, 16, 17, 22, 23, and 25-27 under 35 U.S.C. § 103(a) is respectfully traversed.

B. Claims 1-4, 9-14, 16, 17 and 22-27 are rejected under 35 U.S.C. § 103(a) over a combination of seventeen cited prior art references. The Examiner asserts that this combination of prior art teaches each the elements of the claimed invention aseerted in the rejection above, as well as substitution of PNP/6MPDR for the suicide gene taught in the previous combination of art. As such, the Examiner concludes that the claimed invention would have been *prima facie* obvious to one of skill in the art.

This rejection is respectfully traversed as follows.

The Examiner has not included claims 5, 6, 7 or 8 in this rejection, indicating that each of these claims is non-obvious over the combination of cited art. Since, the claims have been amended to include the limitations of these non-rejected claims, this rejection is rendered moot.

Moreover, as discussed above and as shown in the post-filing publications, the claimed invention provides unexpected therapeutic effect. As such, the claimed invention is not obvious in view of the cited prior at.

Accordingly, the rejection of claims 1-4, 9-14, 16, 17 and 22-27 under 35 U.S.C. § 103(a) over the combined prior at is respectfully traversed.

C. Claims 1-4, 9-14, 16, 17 and 22-27 are rejected under 35 U.S.C. § 103(a) as being unpatentably obvious in view of nineteen cited references, eighteen of which have previously been combined in rejecting a different subset of the claims. The Examiner relies on the nineteenth reference, Xu et al., as teaching an adenovirus vector containing the cell-binding domain of a human type 5 adenovirus. The Examiner concludes that the combination of cited prior art renders the claimed invention *prima facie* obvious.

Applicants respectfully disagree with the Examiner.

This rejection, like the two proceeding rejections of claims under 35 U.S.C. § 103(a) does not include a subset of claims (claims 5-8) whose limitations have been included in the amended claims. As such, this rejection is rendered moot by the amendment of the claims.

Furthermore, as discussed above, the present invention provides unexpected results that could not have been anticipated based on the teachings of the nineteen cited reference. Thus, the rejection of claims 1-4, 9-14, 16, 17 and 22-27 under 35 U.S.C. § 103(a) over the cited combination of art is respectfully traversed.

D. Claims 1-14 and 16-27 are rejected under 35 U.S.C. §103(a) as being unpatentably obvious over the previously combined nineteen prior art references, further in view of Henderson et al. The Examiner relies on Henderson as teaching an adenovirus vector including a probasin promoter and enhancer element. The Examiner concludes, therefore, that it would have been

prima facie obvious to a skilled practitioner at the time of the invention to select each of the elements of the claimed invention and combine them as in the present composition and method to obtain an expected result.

Applicants respectfully disagree with the Examiner's conclusion.

The Examiner has had to combine twenty prior art references to establish this "*prima facie*" case of obviousness. However, the Examiner has merely started with the claimed invention and selected the various elements of the invention from the twenty cited prior art references. This, of course, is not *prima facie* obviousness, but hindsight reconstruction.

Moreover, the combination of cited prior art does not suggest the results obtained with the claimed method and composition. Specifically, the cited prior art does not suggest that the claimed composition and method provide anti-tumor activity in a dose responsive manner as demonstrated in Example 6, and do not suggest that the combination of OAdV plus CS87 plus fludarabidine has significant effect on the growth of prostate cancer cells *in vivo*, as was demonstrated in Example 8.

Accordingly, the rejection of claims 1-14 and 16-27 under 35 U.S.C. § 103(a) over the combined prior at references is respectfully traversed.

E. Claims 1, 2, 9-17 and 22-28 are rejected under 35 U.S.C. § 103(a) as being unpatentably obvious over a combination of all of the previously cited prior art in view of Pramudji et al., Krohne et al. and Ramasamy et al. The Examiner relies on the latter three references as teaching specific promoter, encoding region and poly A sequences to express proteins in various cells. The Examiner concludes, therefore, that combined prior art renders the claimed invention *prima facie* obvious.

This rejection is respectfully traversed as follows.

As with several of the other rejections under 35 U.S.C. § 103(a), this rejection does not include specific claims whose limitations have been incorporated into the amended claims, *i.e.* , claims 6, 7 and 8. AS such, the combined art does not render the claimed invention obvious.

Also, as discussed above, the claimed composition and method provide unexpected anti-cancer activity, which is not suggested by the prior art cited by the Examiner.

Accordingly, the rejection of claims 1, 2, 9-17 and 22-28 under 35 U.S.C. § 103(a) is respectfully traversed.

It is respectfully submitted that the present application, as amended above, is in condition for allowance, an early notification thereof being earnestly solicited. To the extent necessary, a petition for an extension of time under 37 C.F.R. § 1.136 is hereby made.

Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 500417, and please credit any excess fees to such account.

Respectfully submitted,

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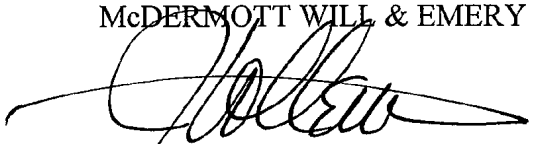

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